We claim:

1. A method for determining if a patient is hypercoagulable, hypocoagulable or normal, comprising:

a) providing a test sample from the patient;

b) initiating coagulation in the sample in the presence of an activator, which is added to the sample in an amount which will result in intrinsic tenase-dependent fibrin polymerization;

c) monitoring formation of said intrinsic tenase-dependent fibrin polymerization over time so as to derive a time-dependent profile, wherein results of said fibrin polymerization monitoring determine whether said patient is hypercoagulable, normal or hypocoagulable.

2. The method according to claim 1, wherein all or part of said time-dependent profile is compared to all or part of a time-dependent profile for a known sample.

3. The method according to claim 2, wherein part of said profile is compared, said part of said profile including one or more of initiation of clot formation, overall change in profile, slope of profile after initiation of clot formation, and acceleration at the time of clot initiation.

4. The method according to claim 2, wherein at least two time-dependent fibrin polymerization profiles are obtained, an additional profile being obtained for a known sample from computer memory or by adding said activator at at least one concentration to a known sample and monitoring the formation of fibrin polymerization over time.

5. The method according to claim 4, wherein at least two time-dependent fibrin polymerization profiles are obtained, one profile for said test sample at a first activator concentration, and at least one additional profile for said test sample at a second activator concentration and/or one or more profiles for a known sample at one or more activator concentrations.

6. The method according to claim 1, wherein the activator comprises tissue factor.

7. The method according to claim 4, wherein at least one parameter from each time-dependent fibrin polymerization profile having varying activator concentrations is determined and a concentration at which the at least one parameter of said sample being tested deviates from normal is determined.

8. The method according to claim 7, wherein said at least one parameter is selected from time index and value of the minimum of the first derivative, the time index and value for the minimum and maximum of the second derivative and the overall magnitude of change.

9. The method according to claim 5, wherein part of each fibrin polymerization profile is compared to a same part of a profile for a known sample.

10. The method according to claim 9, wherein said part is one or more of a time index of the minimum of the first derivative, the value of the minimum of the first derivative, the time index for the minimum of the second derivative, the value for the minimum of the second derivative, the time index of the maximum of the second derivative, the value of the maximum of the second derivative, and the overall magnitude of change.

11. The method according to claim 9, wherein said part is rate or acceleration of fibrin polymerization, wherein said rate or acceleration is compared to rate or acceleration at the same activator concentration for said known sample.

12. The method according to claim 9, wherein a difference or ratio of said parameters for said test sample and said normal sample are determined.

13. The method according to claim 12, wherein said parameter is clot time and a ratio of clot times at different activator concentrations is determined.

14. The method according to claim 1, wherein one or more parameters of said time-dependent fibrin polymerization profile are compared to the same one or more parameters for a normal sample, in order to determine whether said patient is hypercoagulable, normal or hypocoagulable.

15. The method according to claim 7, wherein said at least one parameter includes at least one of time of initiation of clot formation, rate of clot formation, maximum acceleration of clot formation, turbidity at a predetermined time period, and total change in turbidity.

16. The method according to claim 15 wherein said one or more parameters are measures of defects in the thrombin propagation and/or amplification phases.

17. The method according to claim 15, wherein a ratio of said at least one parameter for said test sample to the same parameter for a normal sample is determined.

18. The method according to claim 17, wherein said ratio is determined for multiple concentrations of activator.

19. The method according to claim 18, wherein a concentration at which said ratio departs from 1 is determined.

20. The method according to claim 1, wherein an activator of one or more anticoagulant pathways is added.

21. The method according to claim 20, wherein an activator of protein C is added.

22. The method according to claim 21, wherein the protein C activator is thrombomodulin.

23. The method according to claim 22, wherein a fibrin polymerization profile is obtained with and without said thrombomodulin.

24. The method according to claim 1, wherein multiple concentrations of said activator are used for providing corresponding multiple time-dependent measurement profiles, and multiple concentrations of activator of a known sample are used for providing corresponding multiple time-dependent known sample measurement profiles, and ratios of one or more parameters of the measurement profiles of the known and test sample are compared.

25. The method according to claim 24, wherein the one or more parameters at the one or more concentrations of said activator can be compared in the presence or absence of a modulator of one or more anticoagulant pathways.

26. The method according to claim 1, wherein one or more parameters at multiple concentrations of said activator are determined and results are compared.

27. The method according to claim 24, wherein any concentration of said activator can be compared in the presence or absence of a modulator of one or more anticoagulant pathways.

28. The method according to claim 27, wherein the activator is tissue factor and the modulator is thrombomodulin.

29. The method according to claim 1, wherein the activator comprises tissue factor and phospholipids.

30. The method according to claim 1, wherein a metal salt is added as part of the activator or separately therefrom, which metal salt dissociates into a metal divalent cation when added to the test sample.

31. The method according to claim 30, wherein the divalent metal cation is magnesium, calcium or manganese.

32. The method of claim 30, wherein the metal salt is a halide of magnesium, calcium or manganese.

33. The method of claim 1, wherein the activator comprises purified or recombinant tissue factor.

34. The method of claim 33, wherein the activator comprises homogenized cerebral tissue.

35. The method of claim 1, further comprising adding phopholipids together with or separately from the activator.

36. The method of claim 1, further comprising adding buffers and/or stabilizers to the test sample.

37. The method of claim 1, wherein the test sample is a patient plasma sample.

38. The method of claim 2, wherein the known sample is a normal sample.

39. The method of claim 1, wherein the time dependent measurement profile is an optical absorbance or transmittance profile provided on an automated analyzer.

40. The method of claim 39, wherein a light beam having a wavelength in the visible spectrum is directed through a container holding the test sample and activator, and light absorbed or transmitted is monitored to form the time dependent measurement profile.

41. The method of claim 1, wherein the activator comprises tissue factor sufficiently diluted so as to allow determination of any of hypercoagulable, normal or hypcoagulable depending upon the condition of the patient.

42. The method of claim 1, wherein a part of the time dependent measurement profile other than clot time is compared to the same part of a time dependent measurement profile for a known sample.

43. The method of claim 1, wherein defects in formation of intrinsic tenase complex are detected.

44. The method of claim 1, wherein one or more endpoints from the time-dependent measurement profile are calculated, the endpoints selected from the time of clot initiation and the rate of polymerization.

45. The method of claim 44, wherein at least one parameter selected from the first derivative of the time dependent measurement profile, the second derivative of the time dependent measurement profile, the minimum of the first and/or second derivative, or the maximum of the first and/or second derivative are calculated with respect to value and/or the time associated time index.

46. The method of claim 45, wherein the at least one parameter is compared to the same at least one parameter for a known sample.

47. The method of claim 45, wherein a first ratio is calculated for the at least one parameter at two different concentrations of the activator.

48. The method of claim 47, wherein a second ratio is calculated of said first ratio at the two different activator concentrations relative to a first ratio calculated for a known sample at two different activator concentrations.

49. The method of claim 48, wherein a third ratio is calculated of said second ratio at a first reagent formulation and said second ratio at a second reagent formulation.

50. The method of claim 49, wherein the first reagent formulation comprises a coagulation activator and the second reagent formulation comprises a coagulation activator and an activator of an anticoagulant pathway.

51. The method of claim 50, wherein the first reagent comprises tissue factor and the second reagent comprises tissue factor and thrombomodulin.

52. The method of claim 48, wherein a fourth ratio is calculated of said second ratio calculated for one endpoint relative to said second ratio calculated for a different endpoint.

53. The method of claim 52, wherein one of the endpoints is clot time and the other is the minimum of the first derivative.

54. The method of claim 1, wherein sample is whole blood or platelet rich plasma.

55. The method of claim 1, further comprising adding vesicles to the test sample.

56. The method of claim 55, wherein the vesicles comprise platelets, cellular debris, phospholipid vesicles or platelet microparticles.

57. The method of claim 1, further comprising adding a protein C activator to the test sample.

58. The method according to claim 57, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycolsylated thrombomodulin or fully deglycosylated thrombomodulin.

59. The method of claim 1, wherein the activator comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

60. A method for assessing the coagulation system in a test sample, comprising:

providing a sample to be tested;

adding an activator to said sample to trigger a thrombin explosion dependent on propagation phase and amplification loops and subject to one or more anticoagulant pathways;

measuring the polymerization of fibrin due to said thrombin explosion; and

assessing the coagulation system in said test sample based on said measured fibrin polymerization.

61. The method of claim 60, further comprising adding vesicles to the test sample.

62. The method of claim 61, wherein the vesicles comprise platelets, cellular debris, phospholipid vesicles or platelet microparticles.

63. The method of claim 60, wherein an activator of protein C is added to cause the fibrin polymerization to be sensitive to the protein C pathway.

64. The method according to claim 63, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycolsylated thrombomodulin or fully deglycosylated thrombomodulin.

65.The method of claim 60, wherein the activator comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

66. The method of claim 60, wherein the fibrin polymerization is monitored over time to provide a time-dependent measurement profile.

67. The method of claim 66, wherein an endpoint is extracted from the time-dependent measurement profile.

68. The method of claim 67, wherein the endpoint is normalized by using a model.

69. The method of claim 68, wherein the model is a ratio or difference of the endpoint compared to an endpoint from a time-dependent measurement profile for a known sample.

70. The method of claim 69, wherein the endpoint is initiation of clot formation, overall change in the profile, or slope of the profile after initiation of clot formation.

71. The method according to claim 66, wherein at least two time-dependent fibrin polymerization profiles are obtained, an additional profile being obtained for a known sample from computer memory or by adding said activator at at least one concentration to a known sample and monitoring the formation of fibrin polymerization over time.

72. The method according to claim 71, wherein at least one parameter from each time-dependent fibrin polymerization profile having varying activator concentrations is determined and a concentration at which the at least one parameter of said sample being tested deviates from normal is determined.

73. The method according to claim 67, wherein the endpoint is time index or value of the minimum of the first derivative, the time index or value for the minimum or maximum of the second derivative, or the overall magnitude of change.

74. The method according to claim 66, wherein the rate or acceleration of fibrin polymerization is determined from the time-dependent measurement profile, wherein said rate or acceleration is compared to rate or acceleration at the same activator concentration for a known sample and/or the rate or acceleration of the test sample at a different activator concentration.

75. The method of claim 63, wherein a fibrin polymerization profile is obtained with and without a protein C activator.

76. The method of claim 75, wherein a fibrin polymerization profile is obtained at multiple concentrations of said activator which triggers thrombin explosion.

77. The method of claim 76, wherein a fibrin polymerization profile is obtained at multiple concentrations for a known sample.

78. A method for detecting defects in the propagation and/or amplification phase in the coagulation system of a test sample, comprising:

providing a sample to be tested;

adding an activator capable of triggering a thrombin explosion that is dependent on the propagation phase and/or amplification loops of the coagulation system in the test sample;

measuring fibrin polymerization; and

detecting defects of regulation or modulation in the propagation phase and/or amplification loops in the coagulation system of the test sample based on the measured fibrin polymerization.

79. The method according to claim 78, wherein all or part of said time-dependent profile is compared to all or part of a time-dependent profile for a known sample.

80. The method according to claim 79, wherein part of said profile is compared, said part of said profile including one or more of initiation of clot formation, overall change in profile, slope of profile after initiation of clot formation and acceleration at the time of clot initiation.

81. The method according to claim 79, wherein at least two time-dependent fibrin polymerization profiles are obtained, an additional profile being obtained for a known sample from

computer memory or by adding said activator at at least one concentration to a known sample and monitoring the formation of fibrin polymerization over time.

82. The method according to claim 81, wherein at least two time-dependent fibrin polymerization profiles are obtained, one profile for said test sample at a first activator concentration, and at least one additional profile for said test sample at a second activator concentration and/or one or more profiles for a known sample at one or more activator concentrations.

83. The method according to claim 78, wherein the activator comprises tissue factor.

84. The method according to claim 81, wherein at least one parameter from each time-dependent fibrin polymerization profile having varying activator concentrations is determined and a concentration at which the at least one parameter of said sample being tested deviates from normal is determined.

85. The method according to claim 84, wherein said at least one parameter is time index and value of the minimum of the first derivative, the time index and value for the minimum and maximum of the second derivative and the overall magnitude of change.

86. The method according to claim 82, wherein part of each fibrin polymerization profile is compared to a same part of a profile for a known sample.

87. The method according to claim 86, wherein said part is one or more of a time index of the minimum of the first derivative, the value of the minimum of the first derivative, the time index for the

minimum of the second derivative, the value for the minimum of the second derivative, the time index of the maximum of the second derivative, the value of the maximum of the second derivative, and the overall magnitude of change.

88. The method according to claim 88, wherein said part is rate or acceleration of fibrin polymerization, wherein said rate or acceleration is compared to rate or acceleration at the same activator concentration for said known sample.

89. The method according to claim 88, wherein a difference or ratio of said parameters for said test sample and said normal sample are determined.

90. The method according to claim 89, wherein said parameter is clot time and a ratio of clot times at different activator concentrations is determined.

91. The method according to claim 78, wherein one or more parameters of said time-dependent fibrin polymerization profile are compared to the same one or more parameters for a normal sample, in order to determine whether said patient is hypercoagulable, normal or hypocoagulable.

92. The method according to claim 84, wherein said at least one parameter includes at least one of time of initiation of clot formation, rate of clot formation, maximum acceleration of clot formation, turbidity at a predetermined time period, and total change in turbidity.

93. The method according to claim 92 wherein said one or more parameters are measures of defects in the thrombin propagation and/or amplification phases.

94. The method according to claim 92, wherein a ratio of said at least one parameter for said test sample to the same parameter for a normal sample is determined.

95. The method according to claim 94, wherein said ratio is determined for multiple concentrations of activator.

96. The method according to claim 95, wherein a concentration at which said ratio departs from 1, or a range around 1, is determined.

97. The method according to claim 78, wherein an activator of one or more anticoagulant pathways is added.

98. The method according to claim 97, wherein an activator of protein C is added.

99. The method according to claim 98, wherein the protein C activator is thrombomodulin.

100. The method according to claim 99, wherein a fibrin polymerization profile is obtained with and without said thrombomodulin.

101. The method according to claim 78, wherein multiple concentrations of said activator are used for providing corresponding multiple time-dependent measurement profiles, and multiple concentrations of activator of a known sample are used for providing corresponding multiple time-dependent known sample measurement profiles, and ratios of one or more parameters of the measurement profiles of the known and test sample are compared.

102. The method according to claim 101, wherein the one or more parameters at the one or more concentrations of said activator can be compared in the presence or absence of a modulator of one or more anticoagulant pathways.

103. The method according to claim 78, wherein one or more parameters at multiple concentrations of said activator are determined and results are compared.

104. The method according to claim 101, wherein any concentration of said activator can be compared in the presence or absence of a modulator of one or more anticoagulant pathways.

105. The method according to claim 104, wherein the activator is tissue factor and the modulator is thrombomodulin.

106. The method according to claim 78, wherein the activator comprises tissue factor and phospholipids.

107. The method according to claim 78, wherein a metal salt is added as part of the activator or separately therefrom, which metal salt dissociates into a metal divalent cation when added to the test sample.

108. The method according to claim 107, wherein the divalent metal cation is magnesium, calcium or manganese.

109. The method of claim 107, wherein the metal salt is a halide of magnesium, calcium or manganese.

110. The method of claim 78, wherein the activator comprises purified or recombinant tissue factor.

111. The method of claim 110, wherein the activator comprises homogenized brain tissue.

112. The method of claim 78, further comprising adding phopholipids together with or separately from the activator.

113. The method of claim 78, further comprising adding buffers and/or stabilizers to the test sample.

114. The method of claim 78, wherein the test sample is a patient plasma sample.

115. The method of claim 79, wherein the known sample is a normal sample.

116. The method of claim 78, wherein the time dependent measurement profile is an optical absorbance or transmittance profile provided on an automated analyzer.

117. The method of claim 116, wherein a light beam having a wavelength in the visible spectrum is directed through a container holding the test sample and activator, and light absorbed or transmitted is monitored to form the time dependent measurement profile.

118. The method of claim 78, wherein the activator comprises tissue factor sufficiently diluted so as to allow determination of any of hypercoagulable, normal or hypcoagulable depending upon the condition of the patient.

119. The method of claim 78, wherein a part of the time dependent measurement profile other than clot time is compared to the same part of a time dependent measurement profile for a known sample.

120. The method of claim 78, wherein defects in formation of intrinsic tenase complex are detected.

121. The method of claim 78, wherein one or more endpoints from the time-dependent measurement profile are calculated, the endpoints selected from the time of clot initiation and the rate of polymerization.

122. The method of claim 121, wherein at least one parameter selected from the first derivative of the time dependent measurement profile, the second derivative of the time dependent measurement profile, the minimum of the first and/or second derivative, or the maximum of the first and/or second derivative are calculated with respect to value and/or the time associated time index.

123. The method of claim 122, wherein the at least one parameter is compared to the same at least one parameter for a known sample.

124. The method of claim 122, wherein a first ratio is calculated for the at least one parameter at two different concentrations of the activator.

125. The method of claim 124, wherein a second ratio is calculated of said first ratio at the two different activator concentrations relative to a first ratio calculated for a known sample at two different activator concentrations.

126. The method of claim 125, wherein a third ratio is calculated of said second ratio at a first reagent formulation and said second ratio at a second reagent formulation.

127. The method of claim 126, wherein the first reagent formulation comprises a coagulation activator and the second reagent formulation comprises a coagulation activator and an activator of an anticoagulant pathway.

128. The method of claim 127, wherein the first reagent comprises tissue factor and the second reagent comprises tissue factor and thrombomodulin.

129. The method of claim 125, wherein a fourth ratio is calculated of said second ratio calculated for one endpoint relative to said second ratio calculated for a different endpoint.

130. The method of claim 129, wherein one of the endpoints is clot time and the other is the minimum of the first derivative.

131. The method of claim 78, wherein sample is whole blood or platelet rich plasma.

132. The method of claim 78, further comprising adding vesicles to the test sample.

133. The method of claim 132, wherein the vesicles comprise platelets, cellular debris, lipids or platelet microparticles.

134. The method of claim 78, further comprising adding a protein C activator to the test sample.

135. The method according to claim 134, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycolsylated thrombomodulin or fully deglycosylated thrombomodulin.

136. The method of claim 78, wherein the activator comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

137. A method for determining whether a patient is hypercoagulable, normal or hypocoagulable, comprising:
providing a sample to be tested from a patient;
adding less than 11 picomolar concentration of tissue factor to said sample, said tissue factor generating intrinsic dependent fibrin polymerization in said sample;
measuring formation of the fibrin polymerization; and
determining whether said patient is hypercoagulable, normal or hypocoagulable based on said measured fibrin polymerization.

138. The method according to claim 137, wherein said fibrin polymerization is measured over time so as to derive a time-dependent fibrin polymerization profile.

139. The method according to claim 138, wherein one or more parameters of said fibrin polymerization profile are compared to the same parameters of a fibrin polymerization profile for a normal sample or for the same test sample where the activator or the activator concentration is changed.

140. The method according to claim 139, wherein said one or more parameters do not include clot time.

141. The method of claim 139, wherein the one or more parameters are determined or calculated based on information in the time dependent measurement profiles which are after initiation of clot formation.

142. The method according to claim 141, wherein said one or more parameters include the rate of fibrin polymerization.

143. The method according to claim 137, wherein said sample comprises endogenous or exogenous fibrinogen.

144. The method according to claim 143, wherein the measurement of fibrin polymerization is performed in the absence of a chromogenic substrate in the test sample.

145. The method according to claim 137, wherein the test sample is a non-diluted native plasma sample and the activator added thereto comprises tissue factor.

146. The method according to claim 145, further comprising adding phosphatidylcholine, phosphatidylethanolamine and/or phosphatidylserine as part of the activator or separately therefrom.

147. The method according to claim 137, wherein at least a portion of said time-dependent profile or a value derived therefrom is compared to the same portion or value for a known sample.

148. The method according to claim 147, wherein part of said profile is compared, said part of said profile including one or more of initiation of clot formation, overall change in profile, and slope of profile after initiation of clot formation.

149. The method according to claim 147, wherein at least two time-dependent fibrin polymerization profiles are obtained, an additional profile being obtained for a known sample from computer memory or by adding said activator at at least one concentration to a known sample and monitoring the formation of fibrin polymerization over time.

150. The method according to claim 149, wherein at least two time-dependent fibrin polymerization profiles are obtained, one profile for said test sample at a first activator concentration, and at least one additional profile for said test sample at a second activator concentration and/or one or more profiles for a known sample at one or more activator concentrations.

151. The method according to claim 137, wherein the activator comprises tissue factor.

152. The method according to claim 149, wherein at least one parameter from each time-dependent fibrin polymerization profile at a different activator concentration is determined and a concentration at which the at least one parameter of said sample being tested deviates from normal, or a range around normal, is determined.

153. The method according to claim 152, wherein said parameter is one or more of a time index of the minimum of the first derivative, the value of the minimum of the first derivative, the time index for the minimum of the second derivative, the value for the minimum of the second derivative, the time index of the maximum of the second derivative, the value of the maximum of the second derivative, and the overall magnitude of change.

154. The method according to claim 152, wherein said parameter is rate or acceleration of fibrin polymerization, wherein said rate or acceleration is compared to rate or acceleration at the same activator concentration for said known sample.

155. The method according to claim 152, wherein a difference or ratio of said parameters for said test sample and said known sample are determined.

156. The method according to claim 152 wherein said at least one parameter is a measure of defects in the thrombin propagation and amplification phases.

157. The method according to claim 155, wherein said ratio is determined for multiple concentrations of activator.

158. The method according to claim 155, wherein a concentration at which said ratio departs from 1, or a range around 1, is determined.

159. The method according to claim 137, further comprising adding an activator of one or more anticoagulant pathways.

160. The method according to claim 159, wherein an activator of protein C is added.

161. The method according to claim 160, wherein the protein C activator is thrombomodulin.

162. The method according to claim 161, wherein a fibrin polymerization profile is obtained with and without said thrombomodulin.

163. The method according to claim 137, wherein multiple concentrations of said activator are used for providing corresponding multiple time-dependent measurement profiles, and multiple concentrations of activator of a known sample are used for providing corresponding multiple time-dependent known sample measurement profiles, and ratios of one or more parameters of the measurement profiles of the known and test sample are compared.

164. The method according to claim 137, wherein any concentration of said activator can be compared in the presence or absence of a modulator of one or more anticoagulant pathways.

165. The method according to claim 137, wherein a metal salt is added as part of the activator or separately therefrom, which metal salt dissociates into a metal divalent cation when added to the test sample.

166. The method according to claim 165, wherein the divalent metal cation is magnesium, calcium or manganese.

167. The method of claim 165, wherein the metal salt is a halide of magnesium, calcium or manganese.

168. The method of claim 137, wherein the activator comprises purified or recombinant tissue factor.

169. The method of claim 168, wherein the activator comprises homogenized brain tissue.

170. The method of claim 137, further comprising adding phospholipids together with or separately from the activator.

171. The method of claim 137, further comprising adding buffers and/or stabilizers to the test sample.

172. The method of claim 137, wherein the time dependent measurement profile is an optical absorbance or transmittance profile provided on an automated analyzer.

173. The method of claim 137, wherein the activator comprises tissue factor sufficiently diluted so as to allow determination of any of hypercoagulable, normal or hypcoagulable depending upon the condition of the patient.

174. The method of claim 137, wherein a part of the time dependent measurement profile other than clot time is compared to the same part of a time dependent measurement profile for a known sample.

175. The method of claim 137, wherein defects in formation of intrinsic tenase complex are detected.

176. The method of claim 137, wherein a first ratio is calculated for the at least one parameter at two different concentrations of the activator.

177. The method of claim 176, wherein a second ratio is calculated of said first ratio at the two different activator concentrations relative to a first ratio calculated for a known sample at two different activator concentrations.

178. The method of claim 177, wherein a third ratio is calculated of said second ratio at a first reagent formulation and said second ratio at a second reagent formulation.

179. The method of claim 178, wherein the first reagent formulation comprises a coagulation activator and the second reagent formulation comprises a coagulation activator and an activator of an anticoagulant pathway.

180. The method of claim 179, wherein the first reagent comprises tissue factor and the second reagent comprises tissue factor and thrombomodulin.

181. The method of claim 177, wherein a fourth ratio is calculated of said second ratio calculated for one endpoint relative to said second ratio calculated for a different endpoint.

182. The method of claim 181, wherein one of the endpoints is clot time and the other is the minimum of the first derivative.

183. The method of claim 137, further comprising adding vesicles to the test sample.

184. The method of claim 182, wherein the vesicles comprise platelets, cellular debris, phospholipid vericles or platelet microparticles.

185. The method of claim 137, further comprising adding a protein C activator to the test sample.

186. The method according to claim 185, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycolsylated thrombomodulin or fully deglycosylated thrombomodulin.

187. The method of claim 137, wherein the activator comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

188. A method for monitoring an antithrombotic or procoagulant pharmaceutical therapy, comprising:

providing a first test sample from a patient;

adding an activator to said test sample in order to trigger a thrombin explosion dependent upon the propagation phase and amplification loops of the coagulation system in the test sample;

measuring fibrin polymerization due at least in part to said thrombin explosion;

determining whether the patient is hypocoagulable, normal or hypercoagulable, or providing a baseline;

if the patient is hypercoagulable or hypocoagulable, adminstering one or more antithrombotic or procoagulant pharmaceuticals to said patient;

providing at least one additional sample from said patient at a time after administration of the pharmaceutical;

adding said activator to said at least one additional sample in order to trigger a thrombin explosion dependent upon the propagation phase and amplification loops of the coagulation system in the test sample;

measuring fibrin polymerization in said second sample due at least in part to said thrombin explosion;

determining whether the second patient sample is hypocoagulable, normal or hypercoagulable, or determining a change from baseline; and

determining the effectiveness of the pharmaceutical therapy based on any changes in the hypocoagulability or hypercoagulability from the first test sample, or any changes from baseline.

189. The method of claim 188, further comprising adding vesicles to the test sample.

190. The method of claim 189, wherein the vesicles comprise platelets, cellular debris, phospholipid vesicles or platelet microparticles.

191. The method of claim 188, wherein an activator of protein C is added to cause the fibrin polymerization to be sensitive to the protein C pathway.

192. The method according to claim 191, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycolsylated thrombomodulin or fully deglycosylated thrombomodulin.

193. The method of claim 188, wherein the activator comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

194. The method of claim 188, wherein the fibrin polymerization is monitored over time to provide a time-dependent measurement profile.

195. The method of claim 194, wherein an endpoint is extracted from the time-dependent measurement profile.

196. The method of claim 195, wherein the endpoint is normalized by using a model.

197. The method of claim 196, wherein the model is a ratio or difference of the endpoint compared to an endpoint from a time-dependent measurement profile for a known sample.

198. The method of claim 197, wherein the endpoint is initiation of clot formation, overall change in the profile, or slope of the profile after initiation of clot formation.

199. The method according to claim 194, wherein at least two time-dependent fibrin polymerization profiles are obtained, an additional profile being obtained for a known sample from computer memory or by adding said activator at at least one concentration to a known sample and monitoring the formation of fibrin polymerization over time.

200. The method according to claim 199, wherein at least one parameter from each time-dependent fibrin polymerization profile having varying activator concentrations is determined and a concentration at which the at least one parameter of said sample being tested deviates from normal is determined.

201. The method according to claim 195, wherein the endpoint is time index or value of the minimum of the first derivative, the time index or value for the minimum or maximum of the second derivative, or the overall magnitude of change.

202. The method according to claim 194, wherein the rate or acceleration of fibrin polymerization is determined from the time-dependent measurement profile, wherein said rate or acceleration is compared to rate or acceleration at the same activator concentration for a known sample and/or the rate or acceleration of the test sample at a different activator concentration.

203. The method of claim 191, wherein a fibrin polymerization profile is obtained with and without a protein C activator.

204. The method of claim 203, wherein a fibrin polymerization profile is obtained at multiple concentrations of said activator which triggers thrombin explosion.

205. The method of claim 204, wherein a fibrin polymerization profile is obtained at multiple concentrations for a known sample.

206. A method for evaluating the efficacy of an antithrombotic or procoagulant pharmaceutical, comprising:

providing a first test sample from a human or non-human mammal;

adding an activator to said first test sample in order to trigger a thrombin explosion dependent upon the propagation phase and amplification loops of the coagulation system in the test sample;

measuring fibrin polymerization in the first test sample due at least in part to said thrombin explosion;

determining whether the sample is hypocoagulable, normal or hypercoagulable, or providing a baseline;

administering one or more antithrombotic or procoagulant pharmaceuticals to the mammal;

providing at least one additional sample from the mammal at a time after administration of the pharmaceutical;

adding said activator to said at least one additional sample in order to trigger a thrombin explosion dependent upon the propagation phase and amplification loops of the coagulation system in the test sample;

measuring fibrin polymerization in said at least one additional sample due at least in part to said thrombin explosion;

determining the degree of hypocoagulability or hypercoagulability of the second mammalian sample, or a change from baseline; and

determining the efficacy of the pharmaceutical based on any changes in the hypocoagulability or hypercoagulability from the first test sample, or any changes from baseline.

207. The method of claim 206, further comprising adding vesicles to the test sample.

208. The method of claim 207, wherein the vesicles comprise platelets, cellular debris, phospholipid vesicles or platelet microparticles.

209. The method of claim 206, wherein an activator of protein C is added to cause the fibrin polymerization to be sensitive to the protein C pathway.

210. The method according to claim 209, wherein the protein C activator is purified human thrombomodulin, purified non-human mammalian thrombomodulin, soluble or membrane associated thrombomodulin, native thrombomodulin or thrombomodulin reconstituted with phospholipids, partially or fully glycolsylated thrombomodulin or fully deglycosylated thrombomodulin.

211. The method of claim 206, wherein the activator comprises recombinant or purified tissue factor, truncated tissue factor, or cells expressing tissue factor on their surface.

212. The method of claim 206, wherein the fibrin polymerization is monitored over time to provide a time-dependent measurement profile.

213. The method of claim 212, wherein an endpoint is extracted from the time-dependent measurement profile.

214. The method of claim 213, wherein the endpoint is normalized by using a model.

215. The method of claim 214, wherein the model is a ratio or difference of the endpoint compared to an endpoint from a time-dependent measurement profile for a known sample.

216. The method of claim 215, wherein the endpoint is initiation of clot formation, overall change in the profile, or slope of the profile after initiation of clot formation.

217. The method according to claim 212, wherein at least two time-dependent fibrin polymerization profiles are obtained, an additional profile being obtained for a known sample from computer memory or by adding said activator at at least one concentration to a known sample and monitoring the formation of fibrin polymerization over time.

218. The method according to claim 217, wherein at least one parameter from each time-dependent fibrin polymerization profile having varying activator concentrations is determined and a concentration at which the at least one parameter of said sample being tested deviates from normal is determined.

219. The method according to claim 213, wherein the endpoint is time index or value of the minimum of the first derivative, the time index or value for the minimum or maximum of the second derivative, or the overall magnitude of change.

220. The method according to claim 212, wherein the rate or acceleration of fibrin polymerization is determined from the time-dependent measurement profile, wherein said rate or acceleration is compared to rate or acceleration at the same activator

concentration for a known sample and/or the rate or acceleration of the test sample at a different activator concentration.

221. The method of claim 209, wherein a fibrin polymerization profile is obtained with and without a protein C activator.

222. The method of claim 221, wherein a fibrin polymerization profile is obtained at multiple concentrations of said activator which triggers thrombin explosion.

223. The method of claim 222, wherein a fibrin polymerization profile is obtained at multiple concentrations for a known sample.

224. The method of claim 207, wherein a part of the time dependent profile for each sample is compared to the same part of a time dependent measurement profile for a known sample.

225. A method comprising:
providing a plasma or whole blood sample from a first patient;
adding one or more reagents for activating coagulation, and a metal cation or metal salt which dissociates into a metal cation, and vesicles;
determining that the patient is hypercoagulable or hypocoagulable;
providing a plasma or whole blood sample from a second patient;
adding the one or more reagents comprising the same coagulation activator, metal cation or metal salt, and vesicles as in step (b) to the second patient sample;
determining that the second patient is the other of hypocoagulable or hypercoagulable opposite to the first patient.

226. A method for assessing the hemostatic potential of a sample comprising:

a. providing a sample to be tested;
b. adding a coagulation activator to the sample;

c. generating a time dependent measurment profile; and
d. assessing the hemostatic potential of the sample from the time dependent measurement profile.

227. The method of claim 226, further comprising determining whether the sample is hypocoagulable, normal or hypercoagulable based on the assessed hemostatic potential.

228. The method of claim 226, further comprising determining whether a patient from whom the sample was taken has a thrombotic or hemorhagic tendency.

229. The method according to claim 226, wherein all or part of said time-dependent profile is compared to all or part of a time-dependent profile for a known sample.

230. The method according to claim 229, wherein part of said profile is compared, said part of said profile including one or more of initiation of clot formation, overall change in profile, slope of profile after initiation of clot formation, and acceleration at the time of clot initiation.

231. The method according to claim 229, wherein at least two time-dependent fibrin polymerization profiles are obtained, an additional profile being obtained for a known sample from computer memory or by adding said activator at at least one concentration to a known sample and monitoring the formation of fibrin polymerization over time.

232. The method according to claim 231, wherein at least two time-dependent fibrin polymerization profiles are obtained, one profile for said test sample at a first activator concentration, and at least one additional profile for said test sample at a second

activator concentration and/or one or more profiles for a known sample at one or more activator concentrations.

233. The method according to claim 226, wherein the activator comprises tissue factor.

234. The method according to claim 231, wherein at least one parameter from each time-dependent fibrin polymerization profile having varying activator concentrations is determined and a concentration at which the at least one parameter of said sample being tested deviates from normal is determined.

235. The method according to claim 234, wherein said at least one parameter is selected from time index and value of the minimum of the first derivative, the time index and value for the minimum and maximum of the second derivative and the overall magnitude of change.

236. The method according to claim 232, wherein part of each fibrin polymerization profile is compared to a same part of a profile for a known sample.

237. The method according to claim 236, wherein said part is one or more of a time index of the minimum of the first derivative, the value of the minimum of the first derivative, the time index for the minimum of the second derivative, the value for the minimum of the second derivative, the time index of the maximum of the second derivative, the value of the maximum of the second derivative, and the overall magnitude of change.

238. The method according to claim 236, wherein said part is rate or acceleration of fibrin polymerization, wherein said rate or

acceleration is compared to rate or acceleration at the same activator concentration for said known sample.

239. The method according to claim 236, wherein a difference or ratio of said parameters for said test sample and said normal sample are determined.

240. A method comprising:
providing a test sample from the patient;
initiating coagulation in the sample in the presence of a coagulation activator and optionally an activator of an anticoagulant pathway, the coagulation activator added to the sample in an amount which will result in intrinsic tenase-dependent fibrin polymerization;
monitoring formation of said intrinsic tenase-dependent fibrin polymerization over time so as to derive a time-dependent profile;
looking at an endpoint from the time-dependent profile to assess the hemostatic potential of the test sample.

241. The method of claim 240, further comprising:
repeating steps a) to d) but changing the concentration of the coagulation activator, changing the concentration of the activator of an anticoagulant pathway, and/or changing the endpoint.

242. The method of claim 241, wherein step e) is performed when the first patient sample is hypercoagulable or hypocogulable.

243. The method of claim 242, wherein step e) is performed when the first patient sample is mildly hypercoagulable or hypocoagulable.

244. The method of claim 240 performed on an automated coagulation analyzer.

245. The method of claim 244, wherein the time dependent profile is provided by monitoring light absorbance or transmittance through a cuvette.

246. The method of claim 241, wherein the coagulation activator is tissue factor, the anticoagulant pathway activator is thrombomodulin, and the endpoint is selected from a time index of the minimum of the first derivative, the value of the minimum of the first derivative, the time index for the minimum of the second derivative, the value for the minimum of the second derivative, the time index of the maximum of the second derivative, the value of the maximum of the second derivative, and the overall magnitude of change.

247. The method of claim 241, wherein the endpoint is other than clot time.

248. The method of claim 241, wherein more than one of the concentration of the coagulation activator, the concentration of the activator of an anticoagulant pathway, and the endpoint are altered in step e).

249. The method of claim 241, wherein the endpoint is initiation of clot formation, overall change in the time dependent profile, slope of the profile after initiation of clot formation, and/or acceleration at the time of clot initiation.

250. The method of claim 240, wherein the endpoint is a variable within a curve fit function.

251. The method of claim 188, wherein the fibrin polymerization measurement is used to adjust the patient's therapy to result in a fibrin polymerization profile approximating normal.

252. A method for assessing the hemostatic potential of a sample, comprising:

adding to a sample a coagulation activator, phospholipid vesicles, metal ions or metal salt if the sample is citrated, and optionally an activator of an anticoagulant pathway;

monitoring the polymerization of fibrin in the sample; and

assessing the hemostatic potential of the sample based on the kinetics of the fibrin polymerization;

wherein the coagulation activator is tissue factor sufficiently diluted so as to result in an approximately 0.75 to 3.0 pico molar concentration range when the reagent is mixed with the sample.